## REMARKS

The specification has been amended to insert formal matter and to incorporate the amendments made to the specification in the parent application.

Original claims 1-30 are canceled. New claims 31-38 are being added.

New claims 31-38 are claims copied from U.S. Patent No. 6,444,640, issued September 2, 2002, to Nagane ("the Nagane patent"). The new claims are being presented within one year of the issue date of the Nagane patent, as required under 35 U.S.C. §135(b)(1). A copy of the Nagane patent is enclosed herewith, and listed on the attached Form PTO/SB/08 A & B (modified).

A claim chart (Table I) showing the claims in the Nagane patent, the claims being added in the present application, and the location of support in the present application for the added claims is set forth below.

**Table 1**

| **Nagane claims** (U.S. Patent No. 6,444,640) | **Wiley copy claims** | **Support for Wiley copy claims in the present application** |
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| **1.** Composition useful in treating a condition, comprising (i) a TRAIL molecule and (ii) a DNA damaging agent sufficient to affect apoptosis. | **31.** Composition useful in treating a condition, comprising (i) a TRAIL molecule and (ii) a DNA damaging agent sufficient to affect apoptosis. | "TRAIL may be administered in conjunction with other agents that exert a cytotoxic effect on cancer cells or virus-infected cells" page 34, lines 25-27.<br>"A wide variety of drugs have been employed in cancer treatment. Examples include, but are not limited to, cisplatin[1], taxol, etoposide[2], Novantrone® (mitoxantrone), actinomycin D, camptothecin (or water soluble derivatives thereof), methotrexate, mitomycin (e.g., mitomycin C), dacarbazine (DTIC), and anti-neoplastic antibodies such as doxorubicin and daunomycin" page 34, lines 28-32.<br>"Particular embodiments of the invention are directed to co-administering of TRAIL and methotrexate, etoposide or mitoxantrone to cancer patient..." page 35, lines 13-14. |

[1] Cisplatin is known by those skilled in the art as a "DNA damaging agent." *See, e.g.*, "Platinum anticancer drugs, such as cisplatin, are thought to exert their activity by DNA damage." *Abstract of* Faivre et al., *Biochem. Pharmacol.* 66:225-237 (2003). A copy of the cited abstract is enclosed herewith.

[2] Etoposide is known by those skilled in the art as a "DNA damaging agent." *See, e.g.*, "Etoposide (VP16) is a potent inducer of DNA double-strand breaks (DSBs) and is efficiently used in small cell lung cancer (SCLC) therapy." *Abstract of* Hansen et al., *Int. J. Cancer* 105:472-479 (2003). A copy of the cited abstract is enclosed herewith.

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| **2.** The composition of claim 1, wherein said DNA damaging agent is BCNU, CDPP[3] or VP16. | **32.** The composition of claim 31, wherein said DNA damaging agent is CDDP or VP16. | *Ibid.*, page 34, lines 25-27. "A wide variety of drugs have been employed in cancer treatment. Examples include, but are not limited to, cisplatin[4], taxol, etoposide[5], Novantrone® (mitoxantrone), actinomycin D, camptothecin (or water soluble derivatives thereof), methotrexate, mitomycin (e.g., mitomycin C), dacarbazine (DTIC), and anti-neoplastic antibodies such as doxorubicin and daunomycin" page 34, lines 28-32 (underscore added). "Particular embodiments of the invention are directed to co-administering of TRAIL and methotrexate, etoposide or mitoxantrone to cancer patient..." page 35, lines 13-14 (underscore added). |
| **3.** The composition of claim 1, wherein (i) and (ii) are separated from each other. | **33.** The composition of claim 31, wherein (i) and (ii) are separated from each other. | *Ibid.*, page 34, lines 25-27. *Ibid.*, page 34, lines 28-32. *Ibid.*, page 35, lines 13-14. "As used herein, 'co-administration' is not limited to simultaneous administration. TRAIL may be administered along with other therapeutic agents, during the course of a treatment regime. In one embodiment, administration of TRAIL and other therapeutic agents is sequential" page 36, line 34, through page 37, line 1. |

[3] "CDPP" is incorrectly written. The correct abbreviation is "CDDP" as in claim 8.

[4] CDDP is also known as Cisplatin (*see Abstracts of* Miyatake et al., *Anticancer Res.* 23:2829-2836 (2003) *and* Leitao and Blakley, *J. Otolaryngol.* 32:146-150 (2003)); the chemical name is cis-diamminedichloroplatinum(II). A copy of the cited abstracts is enclosed herewith.

[5] VP16 is also known as Etoposide (*see Abstracts of* Hansen et al., *Int. J. Cancer* 105:472-479 (2003) *and* Demoz et al., *Biol. Chem.* 383:1237-1248 (2002)); the chemical name is 4'-demethylepipodophyllotoxin-9-(4,6-O-(R)-ethylidene-β-D-glucopyranoside). A copy of the cited abstracts is enclosed herewith.

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| **4.** The composition of claim 2, wherein (ii) is present at from about 20-300 $mg/m^2$. | | |
| **5.** A method for treating a subject with a condition that requires affecting apoptosis, comprising administering an amount of the composition of claim 1 to said subject sufficient to affect apoptosis. | **34.** A method for treating a subject with a condition that requires affecting apoptosis, comprising administering an amount of the composition of claim 31 to said subject sufficient to affect apoptosis. | "Properties of the novel cytokine, which is a member of the tumor necrosis factor (TNF) family of ligands, include the ability to induce apoptosis of certain types of target cells. This protein thus is designated TNF Related Apoptosis Inducing Ligand (TRAIL). Among the types of cells that are killed by contact with TRAIL are cancer cells..." page 2, lines 14-18.<br>"The TRAIL protein induces apoptosis of certain types of target cells, such as transformed cells that include but are not limited to cancer cells and virally-infected cells" page 3, lines 23-25.<br>"Among the uses of TRAIL is use in killing cancer cells" page 3, lines 26-27.<br>"Abnormal resistance of T cells toward undergoing apoptosis has been linked to ...development of leukemia, and development of lymphoma" page 32, lines 18-20.<br>"Since TRAIL binds and kills leukemia cells (the Jurkat cell line), TRAIL also may be useful in treating leukemia" page 33, lines 30-31.<br>*Ibid.*, page 34, lines 25-27.<br>*Ibid.*, page 34, lines 28-32.<br>"A method for increasing sensitivity of cancer cells to TRAIL comprises co-administering TRAIL with an amount of a chemotherapeutic anti-cancer drug that is effective in enhancing sensitivity of cancer cells to TRAIL" page 35, lines 10-12.<br>*Ibid.*, page 35, lines 13-14. |

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| **6.** The method of claim 1, wherein said condition is cancer. | **35.** The method of claim 34, wherein said condition is cancer. | *Ibid.*, page 2, lines 14-18.<br>*Ibid.*, page 3, lines 23-25.<br>*Ibid.*, page 3, lines 26-27.<br>*Ibid.*, page 32, lines 18-20.<br>"Since TRAIL binds and kills leukemia cells (the Jurkat cell line), TRAIL also may be useful in treating leukemia" page 33, lines 30-31.<br>*Ibid.*, page 34, lines 25-27.<br>*Ibid.*, page 34, lines 28-32.<br>"A method for increasing sensitivity of cancer cells to TRAIL comprises co-administering TRAIL with an amount of a chemotherapeutic anti-cancer drug that is effective in enhancing sensitivity of cancer cells to TRAIL" page 35, lines 10-12.<br>*Ibid.*, page 35, lines 13-14. |
| | **36.** The composition of claim 31, wherein said condition is cancer. | *Ibid.*, page 34, lines 25-27.<br>*Ibid.*, page 35, lines 13-14. |
| **7.** The method of claim 6, wherein said cancer is glioma. | | |
| **8.** The method of claim 5, wherein said DNA damaging drug is BCNU, CDDP, or VP16. | **37.** The method of claim 34, wherein said DNA damaging drug is CDDP or VP16. | *Ibid.*, page 2, lines 14-18.<br>*Ibid.*, page 3, lines 23-25.<br>*Ibid.*, page 3, lines 26-27.<br>*Ibid.*, page 32, lines 18-20.<br>*Ibid.*, page 33, lines 30-31.<br>*Ibid.*, page 34, lines 25-27.<br>*Ibid.*, page 34, lines 28-32.<br>*Ibid.*, page 35, lines 10-12.<br>*Ibid.*, page 35, lines 13-14. |
| **9.** The method of claim 6, comprising administering said composition intravenously, intraperitoneally, or orally. | **38.** The method of claim 35, comprising administering said composition intravenously. | *Ibid.*, page 2, lines 14-18.<br>*Ibid.*, page 3, lines 23-25.<br>*Ibid.*, page 3, lines 26-27.<br>*Ibid.*, page 32, lines 18-20.<br>*Ibid.*, page 33, lines 30-31<br>*Ibid.*, page 34, lines 25-27.<br>*Ibid.*, page 34, lines 28-32.<br>*Ibid.*, page 35, lines 10-12.<br>*Ibid.*, page 35, lines 13-14.<br>"For therapeutic use, purified proteins of the present invention are administered to |

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| | | a patient, preferably a human, for treatment in a manner appropriate to the indication. Thus, for example, the pharmaceutical compositions can be administered locally, by intravenous injection, continuous infusion, sustained release from implants, or other suitable technique" page 37, line 33, through page 38, line 1. |

No new matter has been added. Entry of the amendment is respectfully requested.

The Examiner is invited to contact the undersigned at his Washington telephone number on any questions which might arise.

Respectfully submitted,

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